INSANITY AND PHTHISIS, THEIR TRANSMUTATION, CONCURRENCE AND CO-EXISTENCE.

By H. A. TOMLINSON, M.D.,

Superintendent St. Peter State Hospital, St. Peter, Minn.

IN 1892 Dr. Thos. J. Mays, of Philadelphia, read a paper before this society, in which he attempted to prove that pulmonary phthisis was essentially a nervous disease. While unable to agree with the conclusion reached by Dr. Mays, I was very much interested in the paper, because my own observation had furnished very similar data; but the conclusion I had drawn, and which I stated in the discussion of the paper, was different. My conclusion was that the concurrence and co-existence of phthisis and insanity indicated an imperfectly developed or unstable organism with a materially lessened power of resistance; and that this hereditary or acquired instability or vulnerability would manifest itself in the lungs of one individual, making him, under proper environment, liable to the development of phthisis; while in another, the instability being in the nervous system, the tendency would be to develop insanity.

In this paper I shall attempt to consider what constitutes this vulnerability, and why there should be such an intimate association between these two conditions, which are not necessarily concomitants, and which as a rule exist independently. However, the offspring of those individuals who are subjects of the tuberculous tendency are very likely to be insane. Indeed, so far as my observation goes, phthisis and insanity are equally potent factors in the production of brain instability.

During the past three years I have made as thorough a study of this subject as was possible with the opportunities afforded, modified, of course, in some cases by want of success in getting detailed information of the life history and hereditary tendencies of the individuals studied. In the beginning I found it useless to attempt to go beyond the time of my personal knowledge of the cases in the hospital, because before that time no effort had been made to get an accurate life history of the individual patient, and there was no record of any physical diseases from which he might have suffered.

During the period since August 1892, out of 695 patients admitted, 70 had a history of phthisis in the family. Thirty-one of these were men, and thirty-nine were women. During this time fifteen men and four women have died from phthisis, and of this number twelve men and one woman were residents of the hospital for a longer period than two years.

The following tables will give the distribution of these cases with regard to hereditary manifestation. In the first tables I have included the admissions in which there was a history of phthisis in the family, and I have dscribed those cases as insanity due to transmutation, in which there is a history of direct or collateral heredity of phthisis, but not of insanity (however in three of the cases a combined heredity existed), while those cases in which phthisis existed in the brothers or sisters of the patient are described as concurrent.

In these tables two general subdivisions have been made. The patients have been classified as primarily degenerate when the insanity has manifested itself before 35 years of age, and progressed steadily toward terminal dementia; as unstable when the degree of defect has not been so great, and the perversion has been temporary, or has made its appearance after middle life, and consecutive to somatic degeneration in some form.

The apparent discrepancy in the figures for degenerate women is due to the fact that some of them had both a direct and collateral heredity.

TRANSMUTATION AND CONCURRENCE.

		Direct.	Collateral.	Paternal.	Maternal.	Concurrent.
Men,	31					
Degenerate,		4	9	6	7	6
Unstable,		8	1	2	7	8
Women,	39					
Degenerate,		14	7	6	12	4
Unstable,		6	6	4	8	5

The preponderence of degeneration among those having an heredity of phthisis is significant, as indicative of the influence of phthisis in one generation, in determining a defective nervous system in the next, and these tables also indicate that the more direct the heredity the greater is the probability of transmutation. The apparent discrepancy between the sexes as to the number in whom the heredity was direct, I cannot explain, but believe it to be accidental. The relatively large number in whom insanity and phthisis was concurrent among brothers and sisters is also of great importance, as showing the intimate association between these forms of degeneration.

The following tables show the co-existence of insanity and phthisis both among the living and the dead, and indicate the time of the tubercular development.

CO-EXISTENCE AMONG THE LIVING.

		At time of Admission.	During First Year.	In Dementia.
Men,	5			
Degenerate,		2	1	1
Unstable,		1		
Women,	7			
Degenerate,			2	3
Unstable,				2

CO-EXISTENCE AMONG THE DEAD.

		At time of Admission.	During First Year.	In Dementia.
Men,	15			
Degenerate,		1	2	7
Unstable				5
Women,	4			
Degenerate,		2		1
Unstable,			1	

With regard to the class of cases figured in these tables it might be well to note here that, like all old-style hospitals, we have the *materies morbi* for tubercular infection always with us, and, as noted, the majority of our cases develop phthisis after coming to the hospital.

The following tables show the form of heredity in those who have died of phthisis, and among those living who are suffering from the disease.

FORM OF HEREDITY IN THOSE DYING OF PHTHISIS.

MEN.				WOMEN.			
Insane Heredity.	Heredity of Phthisis.	Both.	Unknown.	Insane Heredity.	Heredity of Phthisis.	Both.	Unknown.
4			11	1			2

FORM OF HEREDITY IN THOSE LIVING AND SUFFERING FROM PHTHISIS.

MEN.				WOMEN.			
Insane Heredity.	Heredity of Phthisis.	Both.	Unknown.	Insane Heredity.	Heredity of Phthisis.	Both.	Unknown.
1	3		2	3	1	1	4

In those cases in which there is no history of the form of heredity, the presumption, reasoning from analogy, is in favor of an heredity of insanity. It is especially worthy of note in this connection, that of those dying of phthisis not one had an heredity of that disease, while among those living three men and one woman had an heredity of phthisis. Going back to the first tables we find further proof of the transmutation of these two degenerate conditions in the fact that of the seventy cases having an heredity of phthisis only three men and two women have developed the disease.

The three following case records furnish evidence of the co-existence and transmutation of these two diseases, and illustrate the types of defective organization upon which they are engrafted. The record in the cases of the two children is given in detail because they furnish the data for the argument I wish to make as to the nature of the changes which bring these two forms of somatic defect into such intimate association.

The first case illustrates the co-existence of phthisis and insanity in a defective individual in whom the symptoms of active mental perversion were probably antedated by the tuberculous process, although no definite history of the onset could be obtained.

S. O., admitted July 26th, 1892. No history of insanity or phthisis admitted, but the father used alcohol to excess when a young man. The other children, one older and three younger, are healthy, and possess ordinary intelligence. This child was of good disposition before puberty, but since that time has been morose and more or less irritable. She was born in Norway, and came to this country, only a few weeks before admission, with her family. Soon after her arrival her irritability increased, and she became violent. She was nineteen years old when admitted, had menstruated once at the age of fifteen, but not since, and the menstrual molimen was afterward represented by epileptoid convulsions, which continued up to the time of her admission to the hospital. She was quiet and stupid, took no care of herself and had to be fed. About a week after admission she began to cough and had some elevation of temperature. The cough and expectoration increased, the temperature rose steadily, and she began to suffer from diarrhœa and profuse sweating. The temperature reached 105° on the sixth day of her illness, and kept at 103° until she died. The respiration ranged between 34 and 60, and the pulse between 96 and 142, the diarrhœa continued throughout, and the sweating was at all times profuse. No marked symptoms of pulmonary involvement were present at any time during her illness. Her stupidity increased, and finally deepened into coma and death. Died July 25th, 1892.

The postmortem, as was to be expected, disclosed general tubercular involvement. The dura was not thickened, but the subdural space was distended with fluid, especially over the frontal lobes anteriorly. The vessels in the pia were very much injected over the motor area, in the fissure of Sylvius and in the sulci, where the injection was greatest. Numerous small nodular masses were found in the velum interpositum and along the choroid plexuses. The pleura on the left side was adherent throughout the entire surface. In the apex of the left lung were small cavities filled with pus. There were no adhesions on the right side, but at the base of the right lung there was marked hypostatic congestion, and in the middle lobe were several small cavities filled with pus and surrounded by softened tissue. There was an increase of fibroid tissue in both lungs. The mesenteric glands were enlarged, especially in the region of the cæcum. The lower portion of the ileum and cæcum were very much injected, and this portion of the intestine was studded over with enlarged solitary glands, while Peyer's patches were thickened, and in the neighborhood of the cæcum ulcerated. The liver, spleen and kidneys were not involved.

During the past two years I have had an opportunity to study two children of insane parents, who died of tubercular meningitis, and these cases have been of especial interest to me, because they illustrate the two kinds of degeneration that I wish to discuss.

I. C. M. Female. Was born in this hospital May 20th, 1892. Both parents were insane, and the mother had been a dement for some years. The history of the father shows him to have been mentally defective. He had been twice in this hospital, at intervals of a year, suffering from maniacal excitement, which subsided rapidly. He, however, remained unstable for some months afterward in both attacks. He was 23 years old at the time of his first admission, 25 at the birth of the child, and had suffered from two attacks of mental excitement during the preceding five years, beside being incorrigible and very dissipated. This young man was born in Canada, and no history of his family could be obtained; but it was ascertained that his own mental instability began to manifest itself soon after puberty, thus determining its character. Physically he was very robust, and without the slightest indication of organic visceral disease.

The mother, 37 years old at the time of the child's birth, was very robust physically, but had been stupid and demented for a long time. She had always been well physically, but never very bright, and there was a history of collateral heredity, one of the brothers of her mother having been insane.

There was no deformity or apparent asymmetry present at the time of birth in the child, and the mother nursed it during the first eight months of its life. During this time the child was apparently robust, although it was noticed that there was a tendency to disproportionate development of the head, especially in the parietal region. Also that the two sides were not symmetrical, and the vertex was flat. About this time it was also noted that the little girl had a singularly transparent skin, with the superficial veins large and distinctly defined, especially at the temples over the head and on the chest and abdomen.

From its eighth month on, as the mother had ceased to care for it, the little girl was nourished artificially, and although not so robust as formerly was still apparently healthy. The child was singularly beautiful, with large expressive blue eyes, clear transparent skin, rosy cheeks and light hair; its facial expression being what mothers are apt to call "angelic."

The first symptoms noticed in her last illness were an apparent weakness of the legs and an indisposition to walk (she had always been very active). This occurred about the last week in July 1893. During the latter part of the month and the first week in August she would from time to time roll her head in the pillow, usually while lying down and after waking from sleep. This disturbance was at the time attributed to the fact that her molar teeth were at the point of eruption.

Soon after the first symptoms appeared a diarrhœa set in, the stools being fairly consistent, and she also vomitted occasionally at this time. The symptoms did not respond to treatment, and the diarrhœa and vomiting in varying degrees of severity were present during the whole of her illness. Periods of constipation were intercurrent, and for a time the child had colicky pains. On the 6th of August she suddenly became quite stupid, lying quietly with eyes closed, and only looking up after loud calling or persistent effort to attract her attention. This stupor, almost continuous for several days, was later attended by intervals of apparent return of intelligence, when she seemed to recognize those around her. Later there was marked motor disturbance, with rolling of the head and convulsive movements of the limbs; at first limited to the hands and face, but gradually becoming general, when the head and eyes were turned to the left. She also had screaming spells, and moaned a great deal during the last few days. The temperature varied between 101° and 103° F. Pulse between 110 and 160. The respiration was very much accelerated, and examination of the lungs at various times during the last week showed varying rales and irregularity of respiratory murmur. Areas of harshness and impaired resonance were also present. The child was practically unconscious during the last week of its life, with frequent convulsions which occurred as a rule at night. The skin became waxy, and the blood vessels stood out distinctly outlined under the skin. She died August 13th, at 7 A. M.

Autopsy six hours after death. Body pale, waxy in appearance, and very much emaciated. Rigor mortis absent. Cadaveric lividity present, and the fingers and toes cyanosed under the nails. The eyes were sunken, pupils moderately contracted. The anterior fontanelle was present, with the scalp sunken in over it, but the posterior fontanelle had disappeared.

The circumference of the head was 47 cm., occipito-nasion, 29.9 cm., occipito-mental, 51 cm. Bi-mastoid diameter, 30.5 cm., bi-parietal, 18.4 cm., right oblique, from frontal eminence to parietal boss, 24.1 cm., left, 24.8 cm. Length of body, 76.8 cm. There was no asymmetry in body or limbs.

The scalp externally was smooth and free from scars and depressions, but less than the normal amount of hair was present. The scalp was free, smooth on its internal surface, and contained a normal amount of subcutaneous fat.

The skull was smooth, externally and internally the sutures all present, grooves for sinuses and vessels normal, bone thin and elastic, diploe only present in the temporal region. The dura was adherent over the vertex and bulging with fluid. Its external surface was smooth laterally and anteriorly, but rough and thickened over the vertex. The internal surface was smooth but adherent over the right occipital region to the pia-arachnoid, where it was granular in appearance, presenting when separated a surface studded with small white tubercular bodies. The longitudinal sinus was empty, but the lateral sinuses were filled with blood. The quantity of cerebro spinal fluid was 6 oz.

The pia-arachnoid was translucent in general appearance, thickened, and the thickening most marked in the Sylvian fissures. The membrane was very much distended with fluid, and was adherent to the dura at the base anteriorly, where it was very thick and white, being studded with miliary tubercles. The membrane was not adherent to the cortex, but its vessels were enormously distended.

The brain weighed 36 oz. and was softened. 'All over the convexity there were patches of opacity along the vessels, most marked anteriorly and near the median line. The fissures of the median surface were well developed, likewise both Rolandic fissures. The convolutions were simple and the sulci shallow. The simplicity was most apparent in the anterior lobes, while the greatest complexity existed in the parieto-occipital region. The frontal lobes were adherent by their proximal surfaces at the base.

The lateral ventricles were distended, and their ependyma thickened and opaque, but no tubercles were apparent on the surface. The velum interpositum and choroid plexuses were thickened and studded with miliary tubercles. There was a large thick mass extending along the hippocampal lobe on the right side, made up of a cord-like membrane, accompanying the choroid plexus to the base of the brain; apparently an extension inward of the thickened pia at the base. This thickening existed, but only to a slight degree, on the left side.

The corpora quadrigemina were small in proportion to the other nuclei, and the ependyma of the third and fourth ventricles was thickened, opaque, but not roughened. The brain mass was softened and the puncta were well marked. The cortex was thin, pale and translucent, being least well developed in the occipital, thicker in the parietal lobes, and thinner anteriorly. The tracts in the pons and medulla were beautifully defined externally. The pons, medulla, and cerebellum did not share in the softening of the brain mass.

The anterior and posterior mediastinum with the pleural cavities were not diseased. The pericardial cavity contained about 1 oz. of fluid, and its surface was smooth.

The lower lobe of the left lung was congested, and miliary tubercles were present in it and at the apex. The posterior portion of the upper lobe of the right lung was congested, and tubercles were scattered irregularly throughout its substance.

The heart weighed 1½ oz. The left ventricle was thickened, the foramen ovale incompletely closed, and a fat clot filled the right auricle extending into the ventricle.

The omentum was drawn up and shrunken, the mesenteric glands enlarged. The spleen weighed ½ oz., its capsule was adherent, and its substance was studded throughout with miliary tubercles. The liver weighed 12½ oz., and showed no sign of disease. The left kidney weighed 1 oz., its capsule free, the pyramids well marked and the cortex normal. The right kidney weighed ¾ oz., capsule free, pyramids well marked, cortex normal. Both kidneys were lobulated.

I. H.—Born February 9, 1894. Died October 26, 1894. At birth was apparently strong and vigorous; was well nourished and weighed 8½ pounds. Was nursed by mother until the early part of July when he was weaned on account of the mother's failing health, and the consequent poor quality of her milk. When taken from the breast he had considerable elevation of temperature, and for several days thereafter, stools were abnormally frequent, and were green in color. Some premonitory signs of meningeal congestion were present. Artificial feeding was substituted. Upon this he steadily gained and when seven months old, the middle incisors of the lower jaw were erupted without any nervous disturbance. Shortly afterwards he became more fretful, crying a good deal. He took his nourishment in normal amount, however, and temperature remained normal; stools were also normal in character. This condition continued until October 1st, when he became markedly quiet and stupid. Much of the time he lay sleeping, occasionaly waking with two or three short, low outcries, and then falling asleep again. His temperature rose to 100° or 100.5°, and did not vary much from that until October 18th, when it reached 101°. His pulse was somewhat rapid, ranging from 116 to 130, quick in character. On October 18th he had two convulsions both most marked on the left side of the body. The head was turned towards the left side. An alternating strabismus present to slight degree at all times since birth, became exaggerated during convulsive seizures and subsequent stupor. Coarse tremors and irregular muscular contractions were present in the intervals of the convulsions, these movements more pronounced on the left side. From this time onward he took nourishment poorly. Bowels still moved in response to an emulsion of Ol. Ricini.

The day following he had two convulsions in which the twitching was most marked in left arm, and only slight in left leg. Body assumed a position of opisthotonos, and retained it until relaxed in mustard bath. At intervals during the day had tonic spasms, but the clonic movements were absent. On the 20th inst. respiration was irregular, pseudo-Cheyne-Stokes in character; there were four groups of five or six respiratory acts, to the minute, these groups being separated by periods of apnoea. Head was bathed in copious perspiration. Pupils were decidedly unequal, the left being larger. The left eye was in a state of internal squint. Conjunctivæ were not responsive to direct stimulation. Nourishment was taken in very small amount.

October 21st. Marked evidence of effusion, from the distention of the calvarium, bulging at anterior fontenelle. Measurements at this date are as follows:—

Biparietal Diameter	13 cm.
Nasion to Inion	28.5 cm.
Biauricular Line	29 cm.
Left Temp. to R. Par. Boss	20.3 cm.
Rt. Temp. to L. Par. Boss	18 cm.
Circumference through Inion and Nasion	44.2 cm.
Circumference through Obelion and Ment.	49 cm.

At this time both pupils were responsive to light.

From this date onward the emaciation progressed, and the amount of food taken diminished. On the 23d inst. he had a general convulsion, and marked opisthotonos on the 26th inst. His body then became quite cyanotic in appearance, eyes were sunken and extremities cold. The temperature continued to rise higher and was but slightly influenced by the application of cold during the last three days. He died October 26th.

Autopsy:—One hour after death. Body warm and fairly well nourished. The cranial cavity is very much distended and the head gives the sensation of greatly increased weight when held in the hand. A tendency to contracture in the flexor muscles of the fingers persists so that after the fingers are straightened out, they immediately return to a position of contraction with the thumbs drawn into the palm of the hands. The feet were everted, the left more so. There is a tendency toward mottling of the skin, beginning on the inside of the arm and in axilla. (Before the examination was completed this mottling was general over the whole body.) There was no asymmetry of the body except a slight bulging of the chest wall on the right side anteriorly.

The pupils were unequal, the right measuring 4 and the left 5 mm. The eyes were sunken, but this is partly apparent on acccount of the protrusion of the frontal bone. The skull is Brachycephalic and the facial line almost perpendicular. The coronal suture is united but the sagittal and lamboidal are loose, there being a separation of 4 mm. between the parietal bones on the median surface and an overlapping of the occipital by the parietal of 2 cm. Posterior fontanelle absent. Anterior present measuring 4 cm in lateral and 2 mm. in longitudinal diameter. The body measured 69 cm. Circumference of chest 37.5 cm.

Measurement:—Occipito nasion, over convexity 28.2 cm. Circumference 48.2 cm. Bimastoid over vertex 26.5 cm. Verto mental 48.2 cm. From right frontal eminence to parietal boss 17 cm. From left to right 15.2 cm.

The dura was adherent to the bone along the line of the sutures, and in the parietal bones the adhesions extended over most of the surface, also over the frontal parietal and occipital bones on the left side, while on the right side the membrane was free except at the margins of the fissures. The dura in the fossæ was very thick and adherent, especially in the temporal portion of the middle fossa. The dura was generally thickened and its vessels filled with blood. There were 4 oz. cerebro-spinal fluid free in the fossæ and the membrances were all matted together at the base, posteriorly and inferiorly, making it necessary to dissect out with the finger the pons, medulla, and cerebellum.

At the base there was a complete effacement of the superficial anatomical subdivisions, and even the blood vessels were included in the network of new tissue formation in the pia-arachnoid. This extended around the anterior border of the cerebellum and also into the Sylvian fissures, in the left one of which a membranous meshwork was formed 3 mm. in thickness, and which could not be dissected out without tearing the cortex in the region of the operculum and insula. The cranial nerves, where not involved in the new growth, were softened. All of the surfaces described were studded with miliary tubercles varying in size, from 1 to 3 mm., while the pia-arachnoid covering the cortical portions at the base was studded with finely granular tubercles. This same condition existed all over the convexity. Along the median fissure, especially in the frontal and parietal regions, the arachnoid was thickly studded with tubercles, and they extended into the fissure down to the corpus callosum, on the surface of which, and springing from the matted pia-arachnoid, were three tubercles, varying from 1 to 3 mm. in diameter, also numerous granular ones. Over the convexity in the parietal region, and especially on the left side, were numerous creamy patches, but, except in their immediate vicinity, the pia-arachnoid was not thickened, and was opaque only along the vessels.

The principal fissures were illy defined and shallow, and the convolutions were simple, flattened and disposed to be confluent. The lateral and third ventricles were much enlarged and distended. The left had the greatest capacity, and both approximated the size of the ventricles in an adult brain. The ependyma in all of the ventricles presented a granular surface, and the blood vessels were deeply congested. The floor of the fourth ventricle was covered with a filmy meshwork of newly-formed membrane, and this extended along the nerves, having their origin back of the corpora quadrigemina. The velum interpositum and choroid plexuses were adherent, thickened and studded over with granular tubercles, while in the ependyma of the left lateral ventricle over the centre of the caudate nucleus was a tubercle 4 mm. in diameter. The approximate surfaces of the cerebrum, pons, medulla and cerebellum, were matted together, and the membraneous network which united them was filled with granular tubercles. In the centre of the surface of the vermiform lobe was one tubercle which had undergone caseous degeneration, 10 mm. in diameter, and on the lateral lobes on each side were other tubercles, varying from 5 to 8 mm. in diameter.

The brain mass was soft, its cortex varying from 2 to 3 mm. in thickness. The nuclei were as large as are usually found in the ordinary adult brain, and the whole mass weighed 29 oz.

The heart weighed 1 oz. A small amount of fluid in pericardium. No tubercles or inflammatory products, but the coronary vessels were kinked and relaxed. A little fluid blood in left ventricle and a black clot filling the right auriculo-ventricular cavities. The aortic and pulmonary semilunar valves were competent and normal, and the tricuspid and mitral valves appeared normal. Aorta not abnormal in appearance. Heart muscle seemed normal, and so the endocardium.

Right lung weighed 1¾ oz. Strongly adherent at apex. Caseous mass in upper lobe posteriorly 20 mm. in diameter, not broken down. Miliary tubercles scattered through entire lung, especially posteriorly. Left lung weighed 1¼ oz. Miliary tubercles scattered throughout upper and middle portions. Lower lobe most involved.

The spleen weighed ½ oz., and was full of miliary tubercles. Adjacent portion of pancreas also full of them.

Liver weighed 7 oz. Granular tubercles scattered through its substance, Gall bladder distended with bile. Ducts patulous. Supra-renal capsules studded with tubercles. Normal amount of fat about the kidneys, and considerable fat in the walls of the abdomen. Right kidney weighed ¾ oz. There were tubercles scattered over the surface. Capsule free. Left kidney weight 1 oz., presented the same physical characteristics. Bladder distended; did not appear abnormal.

A few granular tubercles in peritoneum, where in contact with liver. The stomach appeared normal. Mesenteric glands enlarged, measuring from 5 to 10 mm. in diameter, and tubercular. The small intestines, especially the jejunum, and also the colon, were studded with tubercles, which in places almost produced strictures of the intestine, forming circles of tubercles around it, and seemed to be ready for ulceration. The diaphragm contained numerous tubercles.

In the case of the first child both parents were typical defectives, and the mother is now a stupid dement with arterio sclerosis developing. The child represented a typical transmutation. Large brain, with excessive development in the parieto-occipital region, mental and physical precocity, and when her illness began, symptoms of cortical irritation from the first with marked and excessive explosions of motor-energy. Again, post mortem, is found destruction of functional tissue rather than excess of tubercular deposit in connective tissue.

In the second child the history of the parents is not definite so far as known. The child was illegitimate, and the woman had given birth to three others, two of whom had died. One is living and robust.

The mother has developed tuberculosis by infection since the birth of this last child.

The life history of this child is exactly the opposite of the first. Stupid and quiet from birth, dull and unintersting, skin thick and coarse, and without color. Signs of degeneration appeared early in twitching and disturbed sleep. The rapid progress of the tubercular disease after its onset, also the enormous effusion, which, however, disappered in part before death. Post mortem, instead of ulceration and destruction of mucous surfaces, an almost universal infiltration of connective tissue with tubercle, also marked connective tissue increase.

Degeneration naturally takes place in connective tissue or epithelial, and is necessarily primarily existent in one or the other. That is, if degeneration begins in an epithelial structure the connective tissue stroma will not undergo degeneration until by contiguity it has become affected (first proliferating and then degenerating because its excessive growth has reduced its potentiality for reconstitution). Also when degeneration begins in a connective tissue, the epithelial tissue is not affected until either mechanically by pressure or indirectly by occlusion of blood vessels and lymph spaces, the nutrition of the epithelial tissue is cut off.

For my purpose in argument I will call degeneration of the epithelial cell—functional destruction, and that of the connective tissue stroma—structural degeneration.

They are both characterized, first by a rapid proliferation of imperfectly formed cells, and finally by destruction of tissue, the nature and product of the destructive process being dependent upon its immediately exciting cause.

Among the insane epithelial degeneration is very uncommon as a primary form, although it can occur in their descendents, as seen in the first child. Among degenerates we find that out of all those subject to infection only a certain number become the victims of tuberculosis; also, it is a well known fact that among victims of phthisis only a small number become insane. Out of 695 cases admitted to this hospital during 2½ years only two men and three women were suffering from phthisis when admitted.

The two children, whose cases are reported, illustrate not only the transmutation from one form of defect to the other, but also the two forms of degeneration, the girl representing the epithelial and the boy the connective tissue type.

In the development of the ovum primarily there is no morphological difference between the cells of the two germinal layers, nor is there anything distinctive at the time of the formation of the mesoblast, and yet from both the inner and outer layers everything that is functional in the organism is developed, while the mesoblast furnishes the framework and connective material for all the organs of the body. The morphological characteristic of all functional tissues of the body is the epithelial cell as the functioning apparatus, and the connective tissue cell as the framework in which it rests. During the physiological activity of a functional tissue the epithelial cell disintegrates being reduced to a simpler form or undergoing retrograde chemical changes. In the connective tissue, however, the process is one of reconstitution *without change of form*, as illustrated in the changes which take place in unicellular organisms. The recent work of Weismann gives an elaborate description of these processes, but from another standpoint.

The epithelial cell is a finished product of organization, and developes into nothing else, although it assumes different forms according to its locality. The connective tissue cell, however, not only undergoes changes in form, but also in structure, so that in its highest stage of development it ceases to have any definite structure or capacity to reproduce itself. Strictly speaking, however, this change from cell to fibril would be one of degeneration, although not of disintegration, such as takes place in the epithelial cell. Now as to the tissues formed by these two types of cell, the epithelial, being the least organized, is the most unstable, being easily broken up with the liberation of considerable energy and the formation of a lower type of cell still more simple and unstable, as illustrated in the cells of the different layers of the cortex. The connective tissue on the contrary is highly organized, stable, not easily affected by incident forces, and having no function in the life processes of the organism; furthermore, the only change it undergoes when deprived of nutrition is liquifaction, as seen in the contents of cysts, especially those occurring in fibroid growth.

It has been my observation, especially among the insane, that disease processes, which are constitutional or diathetic, attack primarily one or other form of tissue with the result of progressive degeneration and disintegration if the tissue be epithelial. However, if the connective tissue is the seat of a diseased process (strictly speaking subject to excessive irritation or withdrawal of nutrition), it either increases rapidly in amount, and remains permanently increased, or undergoes liquefaction.

I have also noticed that among the insane, according to the degree of defect in organization, that there was excessive development of connective tissue with a tendency to rapid proliferation from slight sources of irritation or else extreme response to irritation in epithelial tissue, resulting in rapid disintegration. The most common form of degeneration among the insane is the connective tissue type or the premature and excessive manifestation of the changes, which ordinarily occur in senility. The disproportion between the connective and epithelial tissue constitutes the defect, the amount determines the degree of defect, and its manifestation is in degeneration, as idiocy, imbecility, the higher form, paranoia, or that form represented in those individuals whom Lombroso calls mattoids. In all of these there is a tendency toward premature senility with the development of atheroma, increase of fibroid tissue in all organs and the wasting of epithelial tissue by pressure from encroachment. Of these types the one in which phthisis is most likely to be developed is the lowest grade, the idiot and imbecile, and this is indicated by the statistics of institutions for the care and training of the feeble-minded, which show a large percentage of deaths from phthisis. This is also the case among the insane, and even among those who have remained free from tubercular infection we find, post mortem, marked degenerative change in the pleural cavities and parenchyma of the lung. Out of 111 deaths in this hospital during the biennial period fifteen were from phthisis, thirteen men and two women.

Now what is the biological connection between these two forms of defective development? I have made the statement at different times that I did not believe that the parents should have exhibited a form of defect in order to consider its manifestation in the child as the result of heredity; and that this was especially so in insanity, where the unstable or defective nervous organization of the child may have had for his parental antecedent gout, rheumatism, syphilis, phthisis, or even some profound interference with nutrition during gestation, without the previous existence of any diathetic condition in either parent. I need only add that my further experience confirms this belief.

Next to the functional nerve cell there is no other form of epithelial cell so unstable as that of the functional tissue of the respiratory and digestive apparatus, and then these three are not only more directly and intimately associated, but exist together, even before a circulatory apparatus is developed. In fact the primitive manifestations of life are irritability and respiration.

Although none of the hypotheses concerning heredity and development are fully accepted by all, still they are agreed as to the influence of nutrition and the tendency of parts of the organism to be arrested or limited in their development. As the constituents of the ovum break up into the cell layers, the tendency is to develop in relative proportion. The epiblast and hypoblast appearing sometime before the mesoblast. From the epiblast develops the skin, nervous system, etc. Most authorities also assign the epiblastic layer as the source of the mesoblast, from which in turn develops the connective framework, the circulatory system of the organism, muscles, etc. Now from what we know of heredity, although the direction of development is determined, its completeness is dependent upon nutrition; so that although all parts will exist, if nutrition is imperfect, the most vigorous will develop first and at the expense of the least vigorous; with the tendency for the less vigorous to persist in an imperfect form. This is illustrated in plant life, when if the seed is sown too thickly there is an enormous development of stalk, with only stunted and imperfect grain and if added to this there is not sufficient moisture, the plant will develop prematurely and die without the production of seed.

Now if through any of the numerous causes of impaired nutrition and lowered vitality in one generation, the development of the ovum is interfered with, we find the result in the next generation in the form of the defective individuals I have described; manifesting in various degrees the tendency toward premature senility, with either sterility or the excessive procreation of defective offspring as in plant life. The nervous system and vegetative organs being most highly organized will suffer most, and when the defect is great we will have a preponderence of imperfectly developed connective tissue, while in higher forms there is an excess of epithelial or functional tissue which being imperfectly developed is more unstable and disintegrates more easily. These are the changes which to my mind explain the intimate association of insanity and phthisis and their co-existence; while according to the laws of heredity, the preponderence of imperfectly developed connective tissue in one generation implies the excessive development of functional tissue in the next, thus accounting for the transmutation of disease tendency. These changes are abundantly illustrated in the tuberculous and defective children of neurotic, gouty, or syphilitic parents.

Of course, these processes may be modified in many ways, and I do not include those cases of defective or irregular development which are due to causes operating upon the child during pregnancy, accidents during labor, or the many conditions operating during the two first years of life to produce arrest of development.

The intimate association between phthisis and insanity, however, is certainly significant, and the observations I have made could undoubtedly be paralleled in any institution for the insane. The weak point in the paper is my inability to present a similar series of observations of the nature of the changes found in those dying of phthisis who are not insane, and I have not been able to find anything bearing upon the subject, from this standpoint, with which to compare my observations. The points especially requiring explanation are the infrequency of insanity among victims of phthisis and the nature of the hereditary conditions in these cases. It is certainly a fact that many cases of phthisis, who do not become insane show some of the stigmata of degeneration, but I am debarred from studying this part of the subject in detail. I hope, however, that the subject as I have presented it will interest some of you who may have this opportunity, for I am growing more and more confident that the pathoogly of insanity will only become clear when we fully understand the nature and causes of defective development. It also seems to me highly probable that aside from the asymmetry and undue or imperfect development of the external parts of the body, we have as the principal charactristeic of somatic degeneration excessive growth of connective tissue; while in the higher form of instability or irregular development, the most marked characteristic is excessive development of highly unstable functional tissue easily disintegrated and of limited potentiality, with connective tissue increase as a secondary manifestation.

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